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(71) Applicant *(for all designated States except US)*: **GENENTECH, INC.** [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ACKERLY, Heidi** [US/US]; Box 333, Star Route 2, La Honda, CA 94020 (US). **ASHKENAZI, Avi** [US/US]; 1456 Tarrytown Street, San Mateo, CA 94402 (US). **EBERHARD, David** [US/US]; #212, 360 Guerrero Street, San Francisco, CA 94103 (US). **FRANTZ, Gretchen** [US/US]; 135 San Benito Way, San Francisco, CA 94127 (US). **FRENCH, Dorothy** [US/US]; 318 Beacon Shores Drive, Redwood City, CA 94065 (US). **FUH, Germaine** [US/US]; 149 Amapola Avenue, Pacifica, CA 94044 (US). **HONGO, Jo-Anne** [US/US]; 31 Shaw Court, Redwood City, CA 94061 (US). **LEE, Chingwei** [CN/US]; Apt. 102, 165 Buckingham Way, San Francisco, CA 94132 (US). **MARSTERS, Scot** [US/US]; 990 Cherry Street, San Carlos, CA 94070 (US). **PITTI, Robert** [US/US]; 1110 Liberty Street, El Cerrito, CA 94530 (US). **RAAB, Helga** [DE/US]; 715 Shields Street, San Francisco, CA 94132 (US). **SOROCEANU, Liliana** [RO/US]; Apt. 6, 3042 Sacramento Street, San Francisco, CA 94115 (US). **VARFOLOMEEV, Evgeny** [RU/US]; 7102 Shelter Creek Lane, San Bruno, CA 94066 (US). **WOLF, Beni** [US/US]; 607 Seasons Lane, Redwood City, CA 94065 (US).

(74) Agents: **SHIN, Elinor** et al.; MS 49, 1 DNA Way, South San Francisco , CA 94080-4990 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
16 June 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS RELATING TO STOP-1

(57) Abstract: The present invention provides novel polypeptides, antibodies, antagonists, agonists, potentiators, nucleic acid molecules, compositions and methods relating to the STOP-1 polypeptide that are useful for treating and preventing diseases and for medical diagnosis and research. The present invention also provides consensus sequences and specific sequences for antibodies that specifically bind to STOP-1 that are useful in the methods described herein.

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INTERNATIONAL SEARCH REPORT

Interna[redacted]al Application No
PCT/US2004/011793

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K16/44 C07K14/47 G01N33/53 A61P35/00 C12N15/12
C12N15/63 C12N15/09 A61K31/7088 C07K19/00 C07K16/46
A61K39/395 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, EMBASE, MEDLINE, BIOSIS, CHEM ABS Data, WPI Data, PAJ, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 179 540 A (TAKEDA CHEMICAL INDUSTRIES LTD) 13 February 2002 (2002-02-13) cited in the application example 7 claims 1-8 SEQ ID No. 2 ----- -/--	1,17-22, 27-29, 34, 36-38, 40-43

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 November 2004	11. 03. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Ulbrecht, M

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] in written format

   [X] in computer readable form

   c. time of filing/furnishing

   [ ] contained in the international application as filed

   [ ] filed together with the international application in computer readable form

   [X] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/16602 A (GODDARD AUDREY ; WILLIAMS P MICKEY (US); GENENTECH INC (US); WU THOMAS) 28 February 2002 (2002-02-28) cited in the application page 7, line 15 - page 17, line 15 figure 7 SEQ ID No. 7	1,17-22, 27-29, 34, 41-43, 47,49, 52,54,61
Y		36-38, 40,48, 50,53
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Y		36-38, 40,48, 50,53
X	WO 92/09690 A (GENENTECH INC) 11 June 1992 (1992-06-11) example 11 figures 10,11 claim 46	12,13, 17-22, 27-29, 41-43
Y	WO 00/73346 A (US HEALTH ; PASTAN IRA (US); CHOWDHURY PARTHA S (US)) 7 December 2000 (2000-12-07) page 8, column 23 - column 29 page 40, column 24 - page 45, column 28	36-38, 40,48, 50,53
A	US 5 821 337 A (CARTER PAUL J ET AL) 13 October 1998 (1998-10-13) cited in the application the whole document	1-22, 27-31, 33,34, 36-38, 40-43, 47-54, 61-63,67

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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International Application No
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/011793

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International application No.
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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 47-54,61
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.: 30-33,51,63, 67 (all completely)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-22,34,37,38,47-50,61(all completely);27-29,36,40-43,52-54(all partially)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 47-50 and 61 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
Although claims 51-54 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.1

Claims Nos.: 47-54,61

Claims 47-50,61:
Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body
Claims 51-54:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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Continuation of Box II.2

Claims Nos.: 30-33,51,63, 67 (all completely)

Claims 30-33, 51, 63 and 67 relate to a STOP-1 antagonist and the use thereof, respectively. It cannot be determined which compounds fall under the definition of a STOP-1 antagonist. Although claims 30, 31 and 63 define the binding sit of the said antagonist, the compound is not defined in structural terms. As the said antagonist is not defined, the subject-matter of the said claims is also not defined and a meaningful search of these claims insofar as they relate to said antagonist is not possible (Art. 6 PCT).

Moreover, claim 33 refers to a "stromal targeting agent" which is not clear, thereby further rendering a meaningful search of the scope of said claim impossible (Art. 6 PCT).

Consequently, claims 30-33, 51, 63 and 67 have not been searched.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-22,34,37,38,47-50,61 (all completely); 27-29, 36, 40-43, 52-54 (all partially)

A monoclonal antibody (mAb) that specifically binds to an oligomeric form of human STOP-1; a mAb that specifically binds to amino acids 33-52 or 33-53 of human STOP-1; a mAb that specifically binds to amino acids 94-243 of human STOP-1; a mAb comprising the three amino acid sequences defined in any of claims 5, 9 and 10; a mAb comprising the amino acid sequence of the heavy chain of any of Fig. 27-31 or 34; a mAb having the biological characteristics of a mAb selected from S4, S7, S9, S16, F5 and 6B12; a mAb that specifically binds to STOP-1, wherein the binding of the mAb can be inhibited by a second mAb selected from S4, S7, S9, S16, F5 and 6B12; a mAb that specifically binds to STOP-1, wherein the mAb comprises the light and heavy chain sequences of any S4, S7, S9, S16, F5 and 6B12; a nucleic acid molecule encoding any of said mAbs; a vector comprising said nucleic acid molecule; a host cell comprising said nucleic acid molecule; a composition comprising one of said mAbs; a composition comprising the said nucleic acid molecule; a method for producing any of said mAbs using the said nucleic acid; a method for diagnosing or monitoring a tumour of a patient; a method of inhibiting the growth of a tumour that overexpresses STOP-1 comprising administering to a patient the said mAb composition; a method for determining the presence of a STOP-1 polypeptide in a sample

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2. claims: 23, 24, 55-57 (all completely); 27-29, 35, 36, 39-43, 52-54, 62 (all partially)

A STOP-1 polypeptide variant comprising a STOP-1 polypeptide that cannot be secreted; a nucleic acid encoding the said polypeptide; a vector comprising the said nucleic acid; a host cell comprising the said nucleic acid; a composition comprising said polypeptide; a composition comprising said nucleic acid; a method of producing a STOP-1 polypeptide using the said nucleic acid; a method of inhibiting the growth of a tumour that overexpresses STOP-1 comprising administering to a patient the said composition; a method of inhibiting the growth of a cell that overexpresses STOP-1 comprising the step of inhibiting the secretion of STOP-1 from the cell; an article of manufacture comprising a modified STOP-1 polypeptide or a STOP-1 polypeptide variant

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3. claims: 25, 26, 58 (all completely); 27-29, 35, 36, 39-43, 52-54, 62 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A STOP-1 polypeptide variant that cannot disulfide bind with another STOP-1; a nucleic acid encoding the said polypeptide; a vector comprising the said nucleic acid; a host cell comprising the said nucleic acid; a composition comprising said polypeptide; a composition comprising said nucleic acid; a method of producing a STOP-1 polypeptide using the said nucleic acid; a method for preventing disulfide binding between STOP-1 molecules; a method of inhibiting the growth of a tumour that overexpresses STOP-1 comprising administering to a patient the said composition; an article of manufacture comprising a modified STOP-1 polypeptide or a STOP-1 polypeptide variant

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4. claims: 44-46 (all completely)

A method for producing a STOP-1 polypeptide using a mammalian cell that is deficient in proteoglycan synthesis

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5. claims: 59, 60 (all completely)

A method for cleaving STOP-1 comprising the step of incubating STOP-1 with a protease

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6. claims: 64-66 (all completely)

A method of inducing cell migration in vitro comprising the administration of a STOP-1 polypeptide; a method of testing the activity of a candidate antagonist or agonist of STOP-1 on cell migration

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7. claims: 68-82 (all completely)

A composition comprising an immunoadhesin that comprises a STOP-1 polypeptide and an Fc portion of an antibody; a composition comprising a molecule that potentiates the binding of a STOP-1 polypeptide to a cell surface; an article of manufacture comprising said STOP-1 potentiator or said immunoadhesin; a method of inducing angiogenesis using said STOP-1 potentiator or said immunoadhesin; a method for evaluating/identifying compounds affecting the binding of STOP-1 to cells.
